

CLAIMS

1. Antigenic polypeptide sequence, characterized in that it is the polypeptide sequence of factor VIII.
2. Antigenic polypeptide sequence, characterized in 5 that it lacks the following fragments; alanine 322 - serine 750, leucine 1655 - arginine 1689, lysine 1694 - proline 1782 and aspartic acid 2170 - tyrosine 2332.
3. Sequence according to Claim 1 or 2, characterized in that it is immunogenic.
- 10 4. Sequence according to Claim 3, characterized in that it exhibits an immunoaffinity with inhibitors of factor VIII, preferably with anti-factor VIII antibodies.
5. Sequence according to Claim 3 or 4, characterized in that it exhibits an immunoaffinity for the receptors 15 of T and/or B lymphocytes.
6. Antigenic fragment of the sequence according to Claim 1 or 2, characterized in that it is selected from the group consisting of the polypeptide sequences A1, A2, A3 or C of factor VIII.
- 20 7. Antigenic fragment of the polypeptide sequence A3 according to Claim 6, characterized in that it is selected from the group consisting of the sequence fragment contained between arginine 1652 and arginine 1696, the sequence fragment contained between threonine 25 1739 and aspartic acid 1831 and/or the sequence fragment contained between glutamic acid 1885 and arginine 1917.
8. Sequence epitope of the fragment according to Claim 7, characterized in that it is selected from the group consisting of:
  - 30 - the epitope contained between arginine 1652 and tyrosine 1664, defined by the following sequence:

SEQ ID No:1:

Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr  
1 5 10

- 35 - the epitope contained between aspartic acid 1681 and arginine 1696, defined by the following sequence:

SEQ ID No:2:

Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg  
1 5 10 15

- the epitope contained between threonine 1739  
5 and tyrosine 1748, defined by the following sequence:

SEQ ID No:3:

Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr  
1 5 10

- the epitope contained between asparagine 1777  
10 and phenylalanine 1785, defined by the following  
sequence:

SEQ ID No:4:

Asn Gln Ala Ser Arg Pro Tyr Ser Phe  
1 5

15 - the epitope contained between glutamic acid  
1794 and tyrosine 1815, defined by the following  
sequence:

SEQ ID No:5:

Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro  
20 1 5 10 15  
Asn Glu Thr Lys Thr Tyr  
20

- the epitope contained between methionine 1823  
25 and aspartic acid 1831, defined by the following  
sequence:

SEQ ID No:6:

Met Ala Pro Thr Lys Asp Glu Phe Asp  
1 5

30 - the epitope contained between glutamic acid  
1885 and phenylalanine 1891, defined by the following  
sequence:

SEQ ID No:7:

Glu Thr Lys Ser Trp Tyr Phe  
1 5

35 - the epitope contained between glutamic acid

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1893 and alanine 1901, defined by the following sequence:

SEQ ID No:8:

Glu Asn Met Glu Arg Asn Cys Arg Ala  
1 5

5 - the epitope contained between aspartic acid 1909 and arginine 1917, defined by the following sequence:

SEQ ID No:9:

Asp Pro Thr Phe Lys Glu Asn Tyr Arg  
10 1 5

9. Antigenic fragment of the polypeptide sequence A1 according to Claim 6, characterized in that it is selected between alanine 108 and methionine 355, preferably between alanine 108 and glutamine 228.

15 10. Sequence epitope of the fragment according to Claim 9, characterized in that it is selected from the group consisting of

- the epitope contained between alanine 108 and valine 128, defined by the following sequence:

20 SEQ ID No:10:

Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys  
1 5 10 15  
Glu Asp Asp Lys Val  
20

25 - the epitope contained between glutamic acid 181 and leucine 192, defined by the following sequence:

SEQ ID No:11:

Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu  
1 5 10

30 - the epitope contained between aspartic acid 203 and glutamine 218, defined by the following sequence:

SEQ ID No:12:

Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln  
1 5 10 15

35 - the epitope contained between aspartic acid 327 and methionine 355, defined by the following sequence:

SEQ ID No:13:

Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu  
1 5 10 15  
Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met  
5 20 25

11. Antigenic fragment of the antigenic polypeptide sequence A2 according to Claim 6, characterized in that it is contained between aspartic acid 403 and aspartic acid 725, preferably between histidine 693 and aspartic acid 725.

10 12. Sequence epitope of the fragment according to Claim 11, characterized in that it is selected from the group consisting of:

15 - the epitope contained between aspartic acid 403 and lysine 425, defined by the following sequence:

SEQ ID No:14:

Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg  
1 5 10 15  
Ile Gly Arg Lys Tyr Lys Lys  
20 25

- the epitope contained between valine 517 and arginine 527, defined by the following sequence:

SEQ ID No:15:

25 Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg  
1 5 10

- the epitope contained between histidine 693 and glycine 701, defined by the following sequence:

SEQ ID No:16:

30 His Asn Ser Asp Phe Arg Asn Arg Gly  
1 5

- the epitope contained between serine 710 and aspartic acid 725, defined by the following sequence:

SEQ ID No:17:

35 Ser Cys Asp Lys Asn Thr Gly Asp Tyr Try Gly Asp Ser Tyr Glu Asp  
1 5 10 15

13. Antigenic fragment of the antigenic polypeptide sequence C according to Claim 6, characterized in that it is contained between lysine 2085 and lysine 2249, preferably between lysine 2085 and glycine 2121.
- 5 14. Sequence epitope of the fragment according to Claim 13, characterized in that it is selected from the group consisting of:
- the epitope contained between lysine 2085 and phenylalanine 2093, defined by the following sequence:
- 10 SEQ ID No:18:
- Lys Thr Gln Gly Ala Arg Gln Lys Phe
- 1 5
- the epitope contained between aspartic acid 2018 and glycine 2121, defined by the following sequence:
- 15 SEQ ID No:19:
- Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly
- 1 5 10
- the epitope contained between glycine 2242 and lysine 2249, defined by the following sequence:
- 20 SEQ ID No:20:
- Gly Val Thr Thr Gln Gly Val Lys
- 1 5
15. Major part of the fragments and/or the epitopes according to any one of the preceding Claims 6 to 14, characterized in that it contains the amino acid tyrosine and/or the amino acid histidine linked to at least two other identical or different amino acids.
- 25 16. Conformational epitope, characterized in that it contains at least two different fragments, at least two different epitopes and/or at least two different major parts according to any one of the preceding claims 6 to 15.
- 30 17. Complex comprising a carrier protein or a carrier peptide linked to an element which is selected from the group consisting of the sequence, the fragment, the epitope and/or the major part of an epitope or of a

fragment according to any one of the preceding claims.

18. Inhibitor of factor VIII, characterized in that it exhibits an immunoaffinity with the sequence, the fragment, the epitope, the major part of an epitope or of a fragment and/or the complex according to any one of the preceding claims.

19. Inhibitor according to Claim 18, characterized in that it is an anti-factor VIII antibody or antibody fragment.

10 20. Anti-inhibitor, characterized in that it is directed against the inhibitor of factor VIII according to Claim 18 or 19.

15 21. Anti-inhibitor according to Claim 20, characterized in that it is an anti-anti-factor VIII idiotype antibody or antibody fragment.

20 22. Pharmaceutical composition, characterized in that it comprises at least one element which is selected from the group consisting of the sequence, the fragment, the epitope, the major part, the complex, the inhibitor and/or the anti-inhibitor according to any one of the preceding claims.

25 23. Diagnostic and/or purification device, characterized in that it comprises at least one element which is selected from the group consisting of the sequence, the fragment, the epitope, the major part, the complex, the inhibitor and/or the anti-inhibitor according to any one of the preceding Claims 1 to 21.

30 24. Device according to Claim 23, characterized in that it is a diagnostic kit.

35 25. Device according to Claim 23, characterized in that it is a chromatography column.

26. Use of the pharmaceutical composition according to Claim 22 for preparing a medicament which is intended for the prevention and/or the therapy of immune disorders.

27. Use according to Claim 26, characterized in that the immune disorders are disorders which are induced by inhibitors of factor VIII, inhibitors of the binding of factor VIII to the von Willebrand factor and/or

inhibitors of the binding of factor VIII to membrane phospholipids.

28. Process for the therapeutic treatment and/or prevention of immune disorders, characterized in that the pharmaceutical composition according to Claim 22 is administered to a patient.

29. Therapeutic treatment and/or prevention process according to Claim 28, characterized in that the immune disorders are disorders which are induced by inhibitors of factor VIII, inhibitors of the binding of factor VIII to the von Willebrand factor and/or inhibitors of the binding of factor VIII to membrane phospholipids.

30. Process for identifying and obtaining inhibitors and/or anti-inhibitors according to any one of the preceding claims 18 to 21, characterized in that an element which is selected from the group consisting of the sequence, the fragment, the epitope, the major part and/or the complex according to any one of the preceding claims 1 to 17 is attached to a solid support of a chromatography column, in that a physiological liquid from a patient, which liquid contains inhibitors of factor VIII, is caused to pass through the said chromatography column, in that elution is effected and the fraction containing inhibitors of factor VIII which have exhibited an immunoaffinity with at least one element selected from the group consisting of the sequence, the fragment, the epitope, the major part and/or the complex according to any one of the preceding claims 1 to 17 is collected, and in that, where appropriate, the said process includes the following steps: the said inhibitors of factor VIII which have been collected are attached to the solid support of a chromatography column, anti-inhibitors of factor VIII, such as anti-anti-factor VIII idiotype antibodies, are caused to pass through the said column, elution is effected and the anti-inhibitors having exhibited an immunoaffinity with the inhibitors of factor VIII are collected.

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